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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,073	12/19/2006	Frank Plummer	030841-054132-US	2731

50607 7590 10/28/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/28/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,073	PLUMMER ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *68-81,105-114,121,122 and 129-131* is/are pending in the application.

4a) Of the above claim(s) *74,76 and 78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68-73,75,77,79-81,105-114,121,122 and 129-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/7/07, 11/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office acknowledges the receipt of Applicant's election and Amendment, filed 11 September 2009. Claims 1-67, 82-104, 115-120, 123-128, 132 and 133 have been cancelled. Claims 68-81, 105-114, 121, 122 and 129-131 are pending.

Election/Restriction

Applicant's election without traverse of Group I, claims 68-81, 105-114, 121, 122 and 129-131 in the reply filed on 11 September 2009 is acknowledged.

Applicants' traversal to the sequence election is acknowledged, however, not persuasive. Applicants' argument that the sequences share similarity did not present any issues that materially affect the rationale for the restriction in the prior Office Action.

The instant claims are drawn to multiple oligonucleotides, which are considered to be unrelated, since each sequence claimed is structurally and functionally independent and distinct due to their unique nucleotide sequence and there is no evidence to show significant similarity. As such, the sequences in the instant claims are not considered to constitute a proper Markush group/genus, and are therefore subject to restriction. Furthermore, a search of more than one of the sequences present in these claims presents an undue burden on the Patent and Trademark Office due to the complex nature of the search in terms of computer time needed to perform the search and the subsequent analysis of the search results by the examiner. Each sequence is required to be searched separately due to the difference in the structure and the length.

In view of the foregoing, one sequence is considered to be a reasonable number of sequences for examination.

The requirement is still deemed proper and is therefore made FINAL.

Claims 74, 76 and 78 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected sequence, there being no allowable generic or linking claim. Election was made **with** traverse in the reply filed on 11 September 2009.

In order to facilitate the prosecution of this application, Applicant is requested to consider inserting a claim drawn solely to the above elected sequence and canceling all non-elected embodiments from the claims.

Claims 68-73, 75, 77, 79-81, 105-114, 121, 122 and 129-131 are examined to the extent that they read on the elected sequence, SEQ ID NO:15.

Priority

Acknowledgement is made of Applicant's claim for priority under 35 U.S.C. 119(e) to United States Provisional Application No. 60/466,733 filed 1 May 2003. In light of the fact that the presently claimed subject matter is fully supported by the disclosure of this U.S. Provisional Application, benefit to this earlier filed U.S. Provisional Application has been granted. The effective filing date of the instant application is 1 May 2003.

The disclosure of the prior-filed application, Application No. 60/465783, however, fails to provide adequate support or enablement in the manner provided by the first

paragraph of 35 U.S.C. 112 for the "SEQ ID NO:15" and "microarray" in one or more claims of this application. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Therefore, the priority date of only claims 68, 69, 73, 75, 77, 80, 81, 105, 107-114, 121, 122, 129 and 130 is deemed to have the priority filing date of the current application, 28 April 2003.

Information Disclosure Statement

Applicant's Information Disclosure Statements (IDS) filed 7 May 2007 (six pages total) and 30 November 2006 (three pages total) have each been received and entered into the application. As reflected by the attached, completed copies of form PTO-1449A (nine pages total), the Examiner has considered the cited references.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP §608.01. See pages 21, paragraph [0065], for example.

Claim Rejections - 35 USC § 112, 2nd ¶

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 68-73, 75, 77, 79-81, 105-114, 121, 122 and 129-131 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claims 68, 70, 72, 79, 106, 110 and 112 is a relative term which renders the claim indefinite. The term "substantially pure" or “substantially identical” is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 69, 71, 73, 75, 77, 80, 81, 105, 107-109, 113, 114, 121, 122 and 129-131 are rejected because they depend from indefinite claims.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 112, 1st ¶, enablement

Claims 129 and 130 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id*. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The claims are drawn to a DNA-based SARS-vaccine that expresses SARS proteins. The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

The breadth of the claimed invention is exceedingly large and fails to receive adequate support in the specification. The claims encompass vaccines that prevent infection of any strain of SARS in any subject. The disclosure fails to provide any working embodiments that meet the claimed limitations.

The claims do not provide any structural limitations whatsoever on the immunogenic fragments or epitopes. The specification fails to guide the skilled artisan toward those epitopes that can reasonably be expected to retain the desired protective

immunogenicity. The disclosure also fails to provide any guidance pertaining to the molecular determinants of those regions of the SARS viral envelope and cell surface receptor that are involved in the protection mechanism, which might enable the skilled artisan rationally direct molecules toward certain active sites in the SARS particles. The disclosure is devoid of examples wherein viral titers are measured before and after administration of the SARS-protein-expressing DNA compositions, and measured again after challenge with all prevalent strains of SARS.

The state of the art, at the time of filing, is highly uncertain and unpredictable. The immune pathogenesis of SARS is not well understood. So far, no conclusive information is available on the immune correlates of protection to SARS in patients (Zhi, 2005). CoV replicate by a unique discontinuous transcription mechanism that is not completely understood (Navas-Martin, 2004), which makes it difficult to identify targets for anti-CoV therapeutic agents. More importantly, two major forces drive CoV evolution: recombination and mutation. CoV undergo homologous RNA recombination at high frequencies, although the mechanism is not well understood. It is well known that RNA viruses mutate at rates in the range of 10^{-3} to 10^{-5} base substitutions per nucleotide copied. These values are several orders of magnitude larger than those encountered during replication of DNA viruses, and many orders of magnitude greater than of cellular DNA. As a consequence of this high mutation rate, RNA viruses exist as diverse populations composed of ensembles of closely related, nonidentical genomes that are known as viral quasispecies. The molecular basis of this complexity is the limited copying fidelity exhibited by the viral replicases (Navas-Martin, 2004). As a

result, some of variants will be able to evade the CD8 cytotoxic lymphocytic (CTL) response.

An ideal SARS vaccine should (1) elicit highly potent neutralizing antibody responses against a broad spectrum of viral strains; (2) induce protection against infection and transmission; and (3) be safe by not inducing any infection-enhancing antibodies or harmful immune or inflammatory responses (Jiang, 2005). The guidance presented in the specification is limited to the genome/protein sequence of a novel strain of SARS-CoV. The instant application does not disclose any B cell or T cell ($CD8^+/CD4^+$) epitopes, nor discloses any targets for the neutralizing antibodies, let alone any positive protective immune correlates of any 8000 contiguous nucleotides of SEQ ID NO. In general, both humoral and cellular immune responses are required to protect against CoV (Navas-Martin, 2004). The specification does not teach the immunogenic, pharmaceutical, and vaccine functions of any portion of the 29751 nucleotides of the elected sequence, SEQ ID NO:15, that satisfies the criteria for a SARS therapeutic agent or vaccine as known in the art.

Considering the lack of data or working examples in the specification, the broad scope of the claims, the complex state and nature of the art, and the teachings regarding unpredictability in this art, the Applicant has not provided sufficient information to enable those skilled in the art to make the claimed product without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 68-70, 72, 73, 75, 77, 79-81, 105-113, 121, 122 and 131 are rejected under 35 U.S.C. §102(e) as being anticipated by Rota *et al.* (US 7,220,852 B1, effectively filed 25 April 2003).

The instant claims are directed to a substantially pure SARS virus nucleic acid molecule, comprising a leader sequence and a transcriptional regulatory sequence; a nucleic acid molecule with substantial identity to SEQ ID NO:15; a vector comprising the

nucleic acid molecule; a host cell comprising the vector; a nucleic acid that is complementary or hybridizes substantially to SARS virus nucleic acid; a kit comprising SARS virus nucleic acid; and a microarray comprising a plurality of SARS virus nucleic acid molecules.

The term "a nucleic acid molecule" is interpreted as a portion of the recited SARS coronavirus full-length sequence. The term "substantially identical to … SEQ ID NO:15" reads on any SARS sequence with the same coding proteins.

Rota *et al*. teaches an isolated SARS nucleic acid (column 10, lines 34-67) sequence comprising a leader sequence and a transcriptional regulatory sequence (column 4, lines 29-56), a vector comprising the SARS nucleic acid and transformed into a host cell (column 15, lines 24-29), a kit for detecting SARS in a sample comprising nucleic acid hybridization primers that hybridize to SARS nucleic acid (column 16, lines 53-67), and a microarray comprising array elements comprising SARS virus nucleic acids (column 32, lines 64-68).

Thus, the instant invention is anticipated by Rota *et al*.

Claims 68-70, 72, 73, 79-81, 110-114, 121 and 122 are rejected under 35 U.S.C. §102(e) as being anticipated by Peiris *et al.* (US 7,547,512 B2, priority effective filing date: 24 March 2003 through 25 April 2003).

The instant claims are directed to a substantially pure SARS virus nucleic acid molecule, in particular, with substantial identity to SEQ ID NO:15; a nucleic acid

comprising a sequence that is antisense to SARS virus nucleic acid; and a nucleic acid comprising a sequence that is complementary to SARS virus nucleic acid.

Peiris *et al*. teaches an isolated SARS nucleic acid sequence, or a complement thereof, and an antisense to the SARS virus nucleic acid (column 5).

Thus, the instant invention is anticipated by Peiris *et al*.

Claims 68-70, 72, 73, 79-81, 110-113 and 121 are rejected under 35 U.S.C. §102(a) as being anticipated by Poutanen *et al.* (published online on 31 March 2003).

The instant invention is a substantially pure SARS virus nucleic acid molecule comprising SEQ ID NO:15; and a nucleic acid comprising a sequence that is complementary to SARS virus nucleic acid. The specification discloses that SEQ ID NO:15 is the TOR2 strain isolated from a patient in Toronto, Canada.

Poutanen *et al.* teaches the SARS virus nucleic acid molecules, amplicons, which are synthesized by RT-PCR from respiratory specimens of patients in Toronto, Canada. See page 2002.

Thus, the instant invention is anticipated by Poutanen *et al*.

The limitations "wherein said molecule comprises a s2m motif" in present claim 73 and “wherein said vector is a gene therapy vector” in present claim 107 have been considered, but it is noted that the phrase “gene therapy” is a recitation of the intended use or function of the claimed vector, whereas the phrase "s2m motif" is a recitation of

the property of the SARS nucleic acid structure, and fails to impart any physical or structural property to the medicament. Thus, present claims 73 and 107 read on any SARS virus nucleic acid molecules. The cited prior art meet this limitation because all of them teach SARS virus nucleic acids.

Conclusion

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the application as filed so as not to add new matter. See MPEP §714.02 and §2163.06.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

14 October 2009